

## REMARKS

1. According to the appeal comments, this amendment adds the limitation of “the isolated mesenchymal stem cells proliferate without differentiation and reach confluence after several passages” in Claim 1. This application disclosed that “in one preferred embodiment of the present invention, the isolated mesenchymal stem cells proliferate without differentiation and reach confluence even after 12 passages. The unexpected results was supported by post-filing art (Kato et al US Patent Application 20050013804, filling date: 09/12/2001), which mentioned that “The conventional culture methods however cannot produce sufficient amounts of mesenchymal stem cells because the proliferation of said stem cells stops or becomes extremely slow around 15<sup>th</sup> generation.”
2. Mussi et al. disclose a device of trans-membrane co-culture of cells, which requires a “inverting” procedure. The US patent 5409829 describes that “the system is then inverted and first lid 58 is removed.” (Column 5 lines 31-32) Moreover, the ‘829 patent also needs additional lid and plug. In other words, not only the procedure but also the structure are quite different from this application. Thus, one of ordinary skill in the art could not combine the teaching of Mussi et al with those of Caplan and Barkitt in the way of this application.

Furthermore, the ‘829 patent was criticized by other inventors. US Patent 5710043 discloses that “the cell culture system disclosed in Ser. No. 08/124,415, now U.S. Pat. No. 5,409,829, is well suited to culture cells on both sides of a membrane, but the distance is fixed and the system requires a series of manipulations that may be time consuming for screening studies where multiple co-cultures are being developed.” (Column 2 lines 3-7) Therefore, one of ordinary skill in the art could not have the motivation to combine the teaching of Mussi et al with those of Caplan and Barkitt.

3. This applicants have not noticed the prior art of Mussi et al before, because they thought Mussi as a typo of Matsui.

Accordingly, this application should be placed in condition of allowance. An early Notice to this effect is respectfully expected.

Respectfully submitted:

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